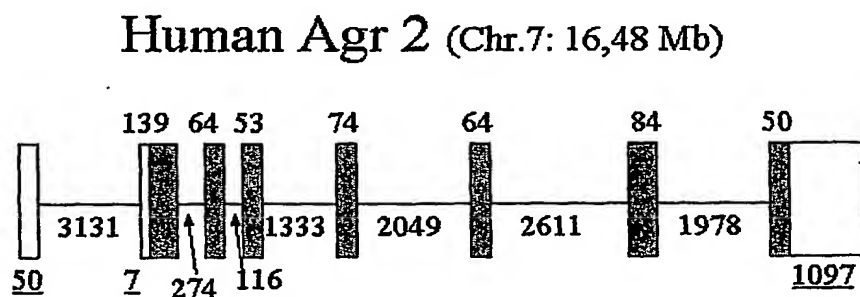
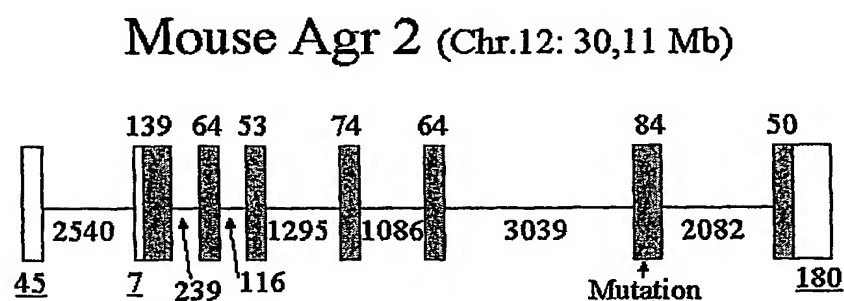


Figure 1A.

Mouse Gene ID	Mouse Gene Description	Chr	Map Start	Human Gene ID	Human Gene Description	Chr	Map Start
Q92324	NEPHRIN OF ATONAL 3	12	28041829	Q96R16	NEPHRIN OF ATONAL 3	7	18829031
NH 011658	TWIST RELATED PROTEIN (H-TWIST)	12	28071270	TWIST	TWIST RELATED PROTEIN (H-TWIST)	7	18800882
NH 024124	HISTONE DEACETYLASE 9 (HD9) (HD7B)	12	28488280	NH 014707	HISTONE DEACETYLASE 9 (HD9) (HD7B) (HD7)	7	18179912
NH 013464	AH RECEPTOR PRECURSOR (AHR)	12	29623298	AHR	AH RECEPTOR (ARYL HYDROCARBON RECEPTOR) (AHR)	7	16982797
BC023499	SIMILAR TO ANTERIOR GRADIENT PROTEIN 3	12	30054071	Q8TD06	ANTERIOR GRADIENT PROTEIN 3	7	16543709
Q86912	ANTERIOR GRADIENT PROTEIN 2 (HOMOLOG OF XENopus LARVIS)	12	30112578	Q86912	ANTERIOR GRADIENT PROTEIN 2 (HOMOLOG OF XENopus LARVIS)	7	16426072
HOMX2 MOUSE	HOMEOBOX PROTEIN HOX-2	12	31233665	HOMX2	HOMEOBOX PROTEIN HOX-2	7	15295209
NH 007960	ETS1 PROTEIN (ETS TRANSLOCATION VARIANT 1)	12	32910756	ETV1	ETS TRANSLOCATION VARIANT 1 (ETS1 PROTEIN)	7	13579610
NH 007487	ADP-RIBOSYLATION FACTOR-LIKE PROTEIN 4	12	34165437	ARL4	ADP-RIBOSYLATION FACTOR-LIKE PROTEIN 4	7	12370905
NH 009132	ADSEVERIN (SCINDERIN) (GELSOLIN-LIKE PROTEIN)	12	34189389	Q96PT2	ADSEVERIN (SCINDERIN)	7	12254575

Figure 1B.



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Figure 2.

BLAST 2 Sequences

(<http://www.ncbi.nlm.nih.gov/blast/bl2seq/bl2.html>)

Sequence 1: mouse AGR2 (WT); SEQ ID No:3

Sequence 2: human AGR2 (WT); SEQ ID No:4

NOTE: The statistics (bitscore and expect value) is calculated based on the size of nr database.

Score = 323 bits (828), Expect = 4e-88.

Identities = 160/175 (91%), Positives = 168/175 (95%)

```
Query: 1  MEKFSVSAILLLVAISGTLAKDTTVKSGAKKDPKDSRPKLPQTLSRGWDQLIWTQTYEE 60
          MEK  VSA LLLVA+S TLA+DTTVK GAKKD KDSRPKLPQTLSRGWDQLIWTQTYEE
Sbjct: 1  MEKIPVSAFLLLVALSYTLARDTTVKPGAKKDTKDSRPKLPQTLSRGWDQLIWTQTYEE 60

Query: 61  ALYRSKTSNRPLMVIHHLDECPHSQALKKVFAEHKEIQKLAEQFVLLNLVYETTDKHLSP 120
          ALY+SKTSN+PLM+IHHLDECPHSQALKKVFAE+KEIQKLAEQFVLLNLVYETTDKHLSP
Sbjct: 61  ALYKSKTSNKPLMIIHHLDECPHSQALKKVFAENKEIQKLAEQFVLLNLVYETTDKHLSP 120

Query: 121 DGQYVPRIVFVDPSLT77VRADITGRYSNRLYAYEPSDTALLYDNMKKALKLLKTEL 175
          DGQYVPRI+FVDPSLT77VRADITGRYSNRLYAYEP+DTALL DNMKKALKLLKTEL
Sbjct: 121 DGQYVPRIMFVDPSLT77VRADITGRYSNRLYAYEPADTALLLDNMKKALKLLKTEL 175
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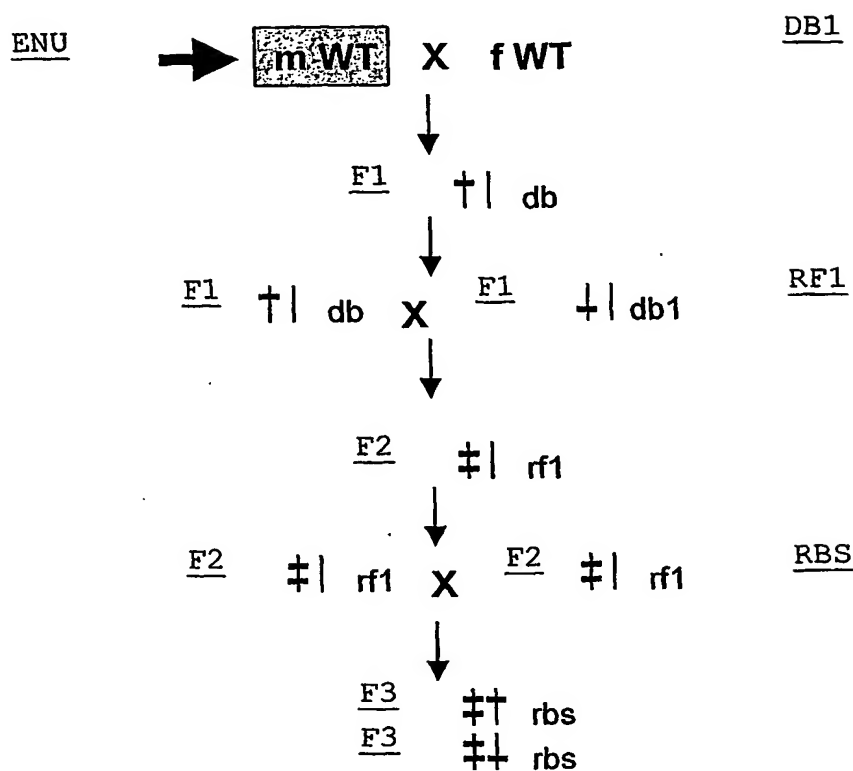
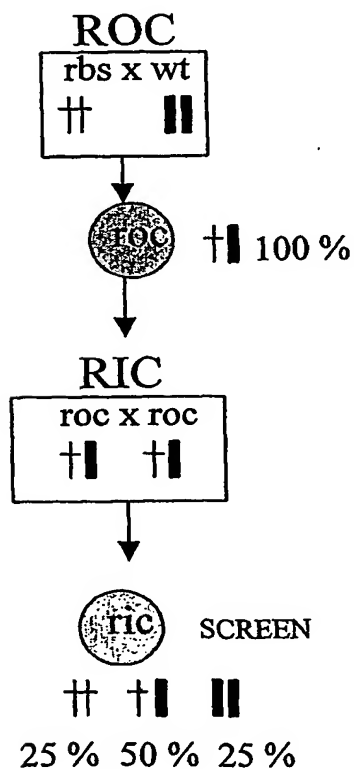
Figure 3.**Breeding-Scheme:**
A) F3 production**B) Outcross**

Figure 4.

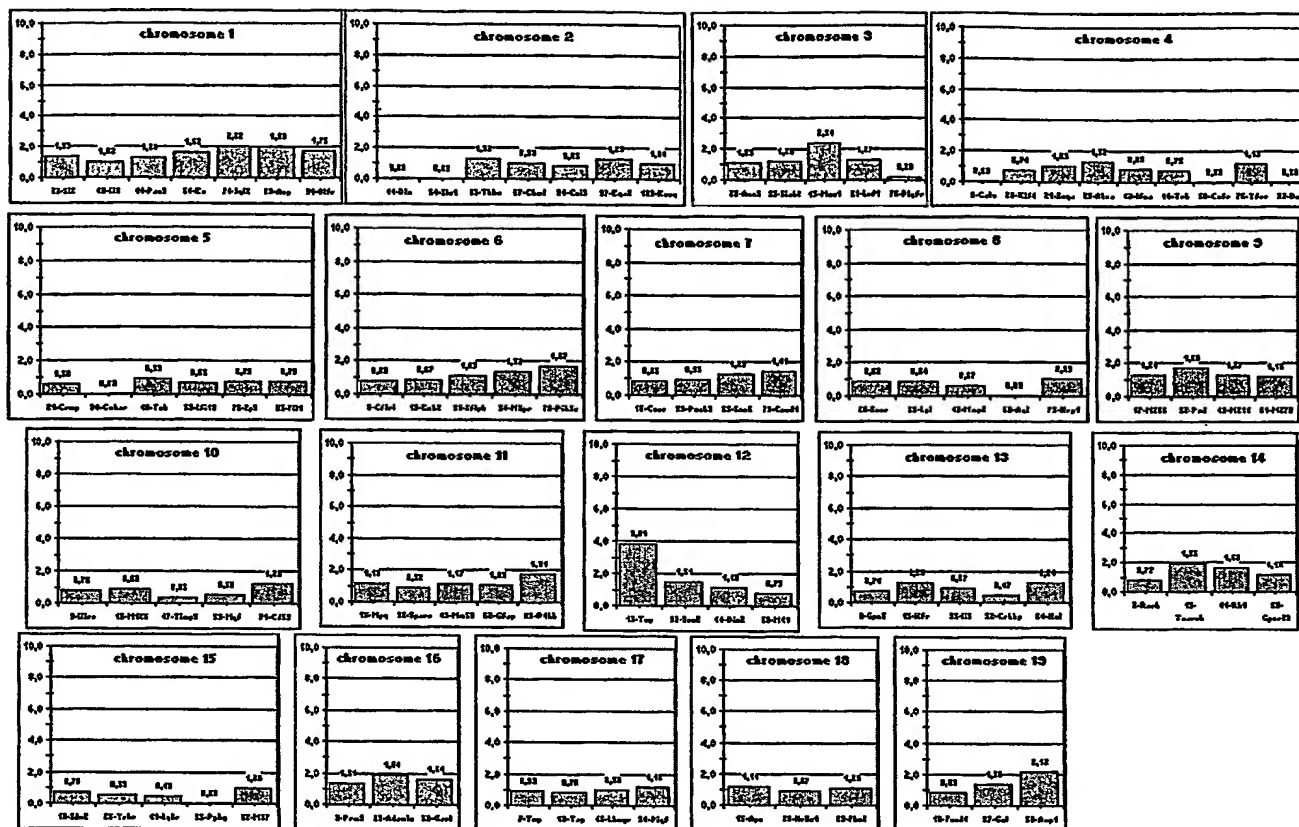


Figure 5.**Haplotypes Scheme**

























appr. cM	Marker	appr. Mb			
6	D12Mit12	18,7			
7	Idb2	19,1			
<hr/>					
10	D12Mit171	23,4			
8	Slc26a3	25,5			
14	D12Mit221	40,3			
<hr/>					
18	D12Mit64	44,8			
19	D12Mit110	46,3			
25	D12Mit285	49,1			
			SEX	m	f
			MOUSE	#899	#99
					m
					#64

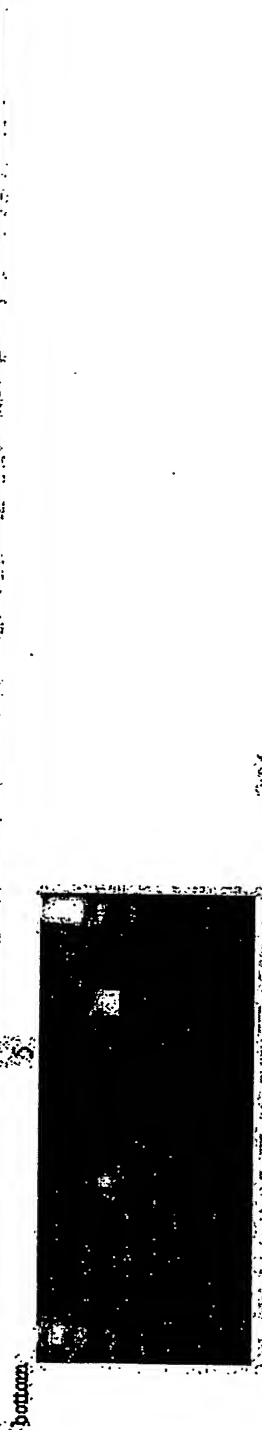
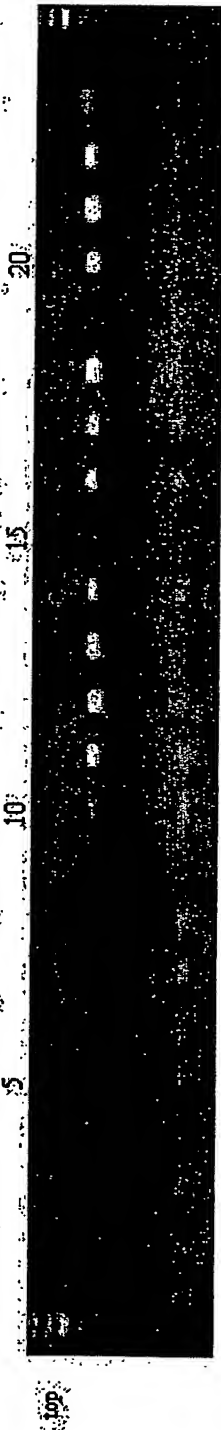
Figure 6

primer: Mm Arg2-7/2 (349 bp)

project: mAg2

gender specific female organs + embryo

Tissue cDNA panel C3H male



- | | | | | |
|-------------------------------|--------------------|------------------|----------------------|------------------------|
| top | 1 total brain | 13 thyroid gland | 13 ovary | bottom |
| 2 olfactory lobes | 14 lung | 14 lymph nodes | 14 uterus | 1 Marker 100 bp ladder |
| 3 cerebellum | 15 tongue | 15 mesenterium | 15 placenta | 2 Embryo d 13.5 head |
| 4 cerebellum left hemisphere | 16 esophagus | 16 gall bladder | 16 sternum | 3 Embryo d 13.5 body |
| 5 cerebellum right hemisphere | 17 salivary gland | 17 liver | 17 bone marrow | 4 Embryo d 18.5 head |
| 6 cerebellum | 18 stomach | 18 spleen | 18 whole blood | 5 Embryo d 18.5 body |
| 7 pituitary gland | 19 pancreas | 19 kidney | 19 skin | 6 pool |
| 8 mesencephalon | 20 small intestine | 20 adrenal gland | 20 adipose tissue | 7 neg. control |
| 9 mesencephalon | 21 large intestine | 21 bladder | 21 skeletal muscle | 8 Marker 100 bp ladder |
| 10 eye | 22 appendix | 22 testis | 22 ES cells | |
| 11 nose and pharynx | 23 rectum | 23 epididymis | 23 Embryo d 5.5 | |
| 12 trachea | 24 thymus | 24 prostate | 24 Embryo d 9.5 | |
| | | | Marker 100 bp ladder | |

Figure 7.

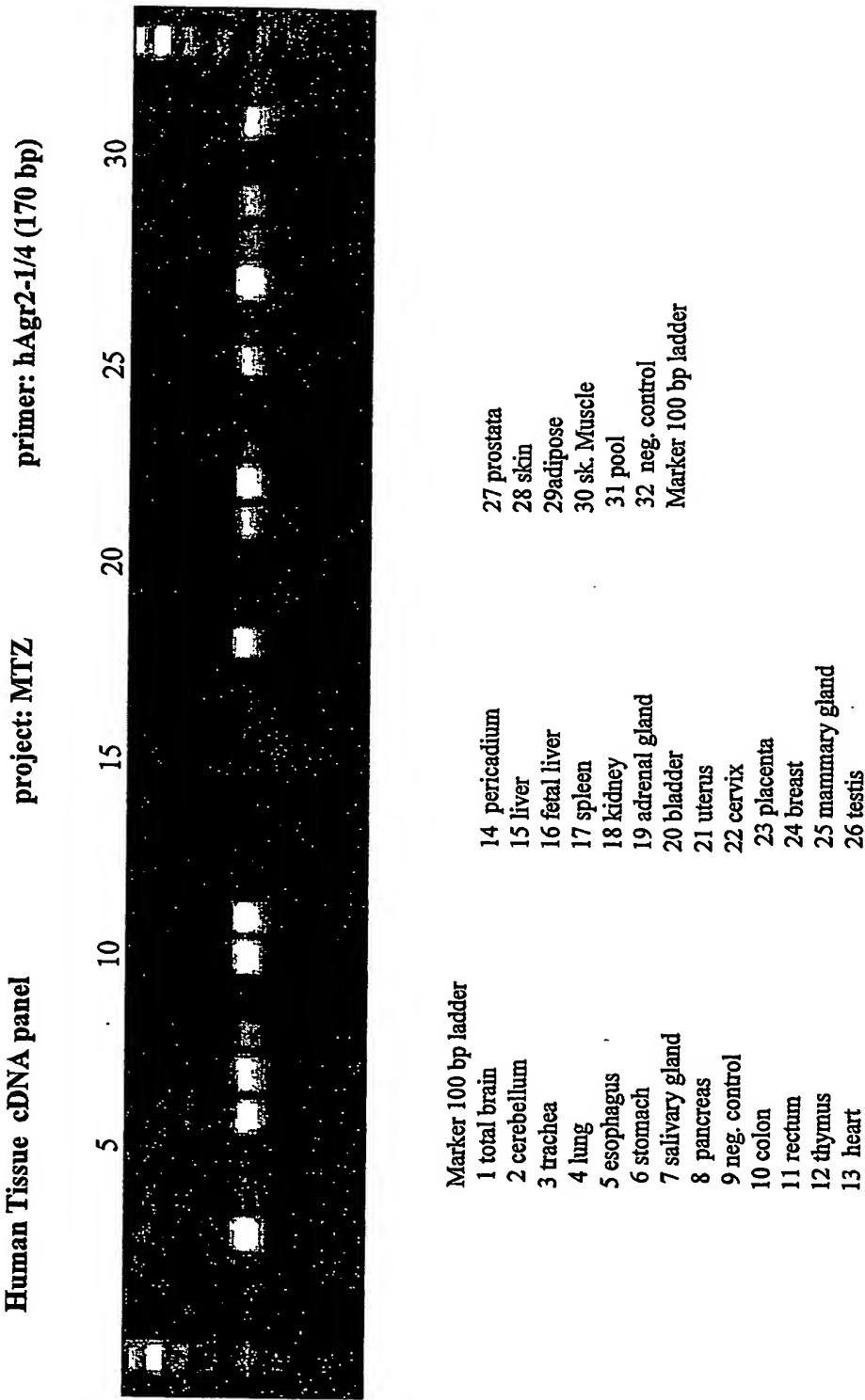


Figure 8.

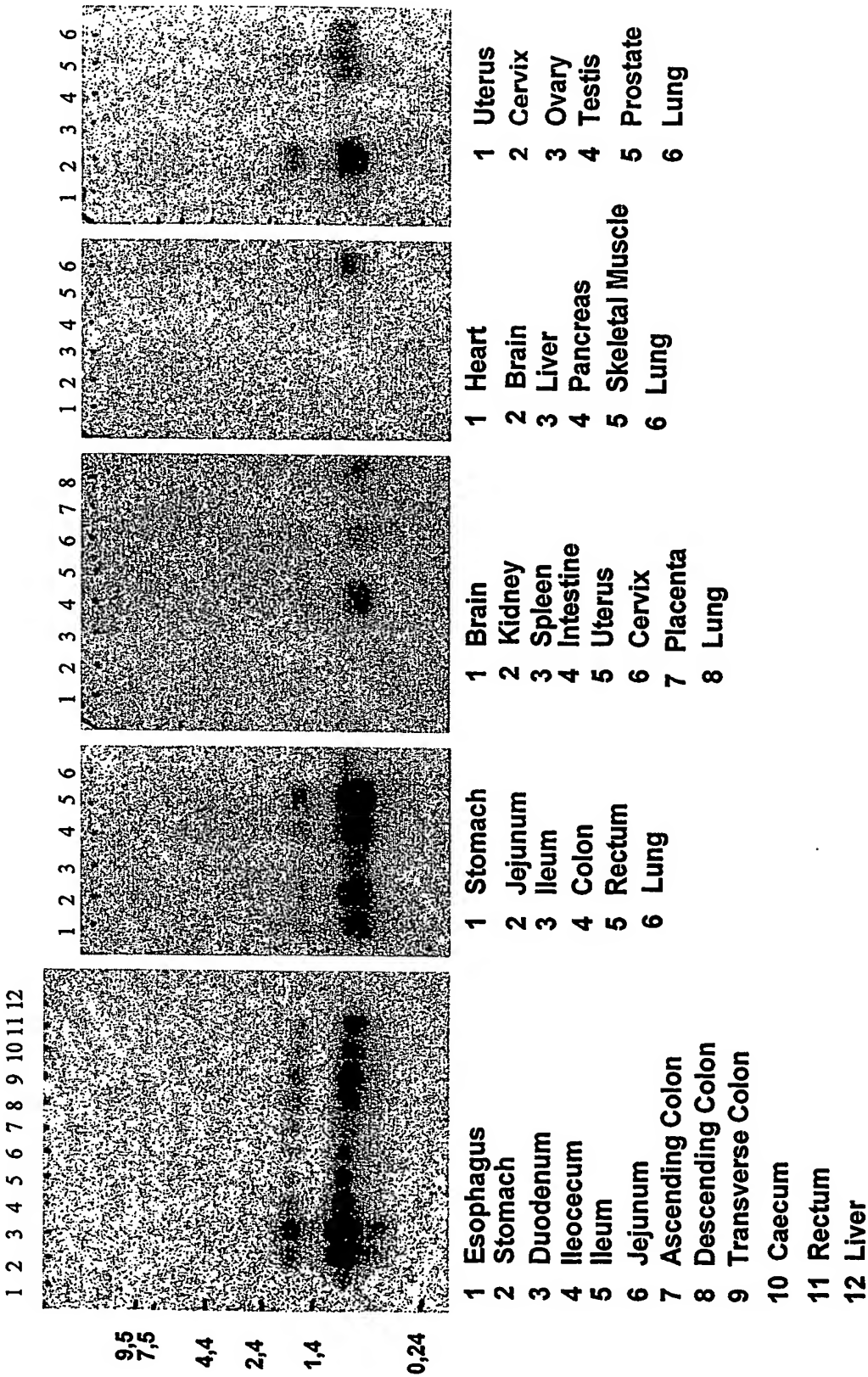


Figure 9.

mouse number	agr2 genotype	thriving deficit	chronic diarrhea
1	mut	yes	yes
2	mut	yes	yes
3	mut	yes	yes
4	mut	yes	yes
5	mut	yes	yes
6	hz	no	no
7	hz	no	no
8	hz	no	no
9	hz	no	no
10	hz	no	no
11	hz	no	no
12	hz	no	no
13	hz	no	no
14	hz	no	no
15	hz	no	no
16	hz	no	no
17	hz	no	no
18	hz	no	no
19	wt	no	no
20	wt	no	no
21	wt	no	no
22	wt	no	no
23	wt	no	no
24	wt	no	no
25	wt	no	no

Figure 10.

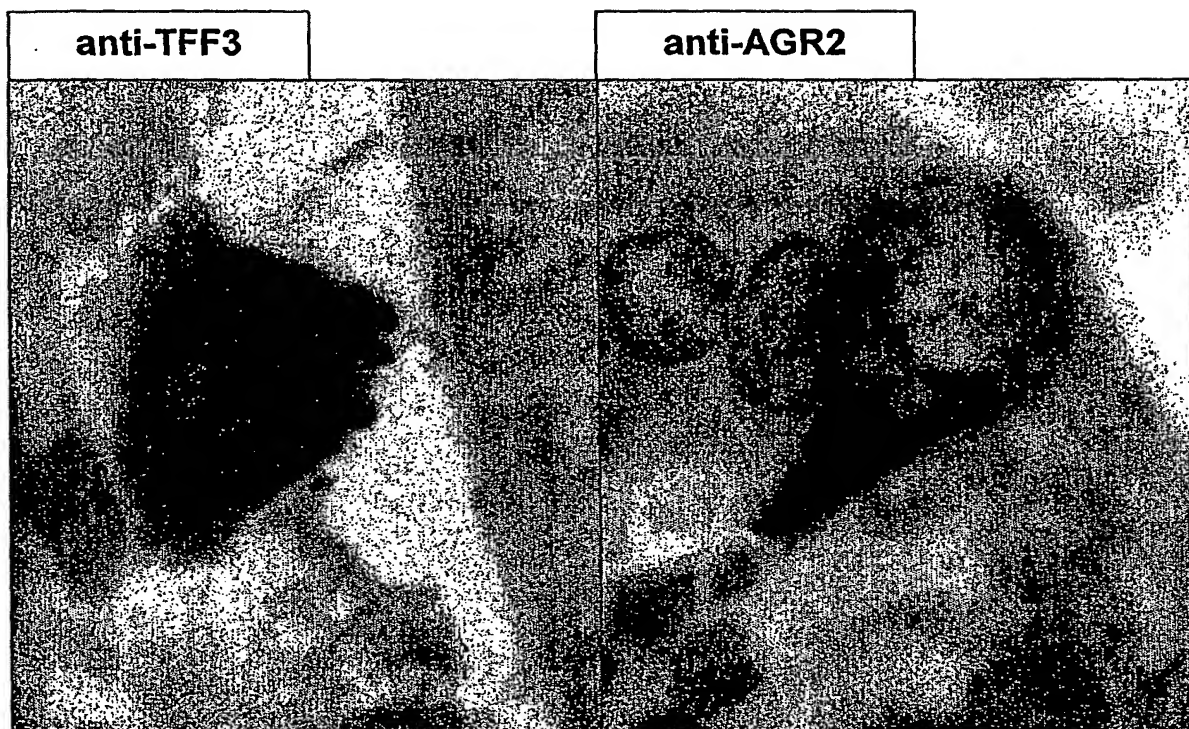


Figure 11.

Colon (wild type mouse)



Colon (affected mouse)



Figure 12.

Colon (affected mouse)

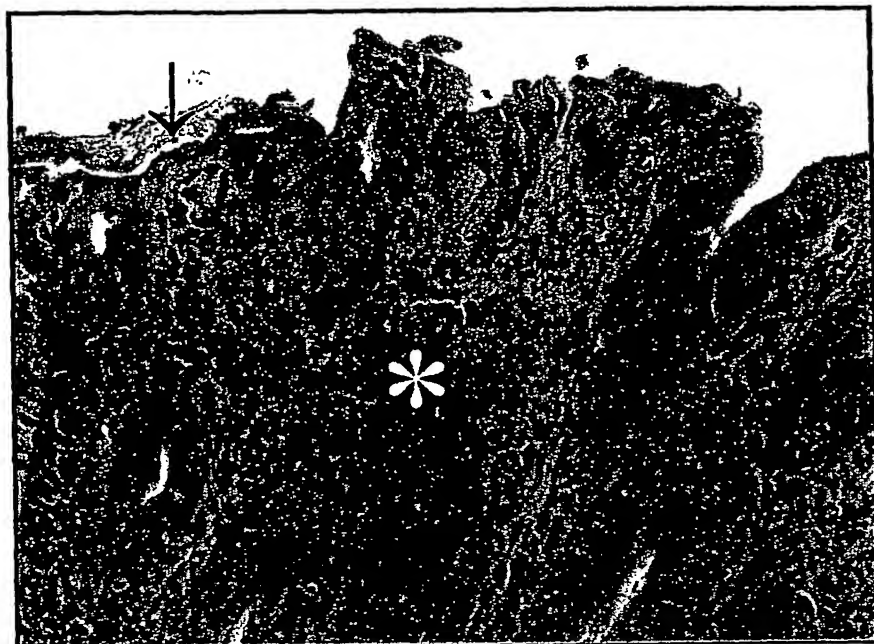
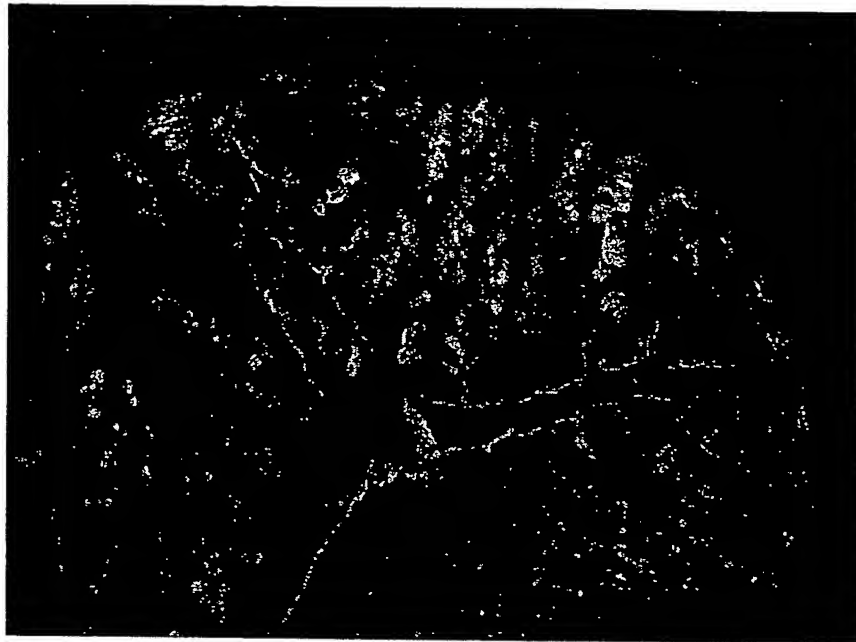


Figure 13.

Colon (wild type mouse)

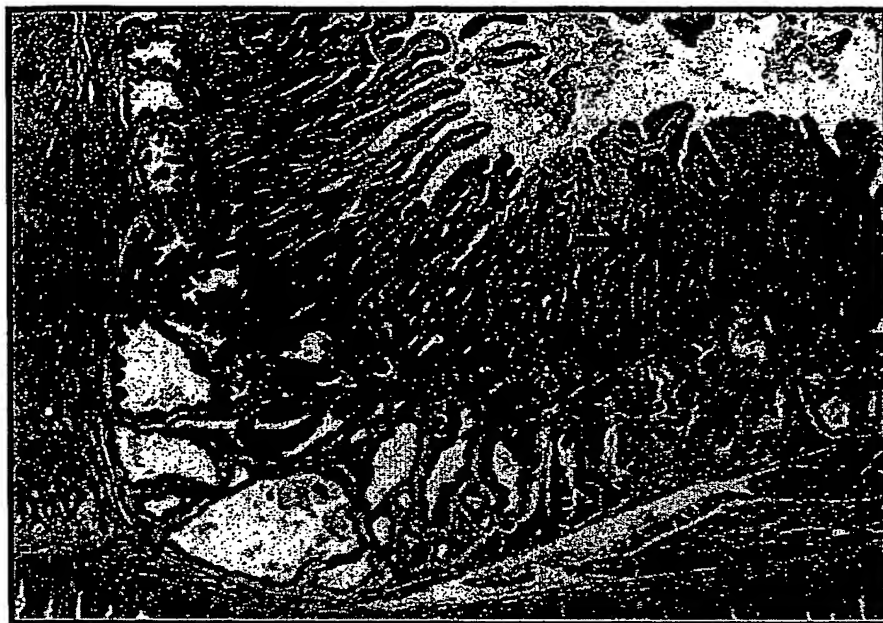


Colon (affected mouse)



Figure 14.

Brunner's gland (wild type mouse)



Brunner's gland (affected mouse)



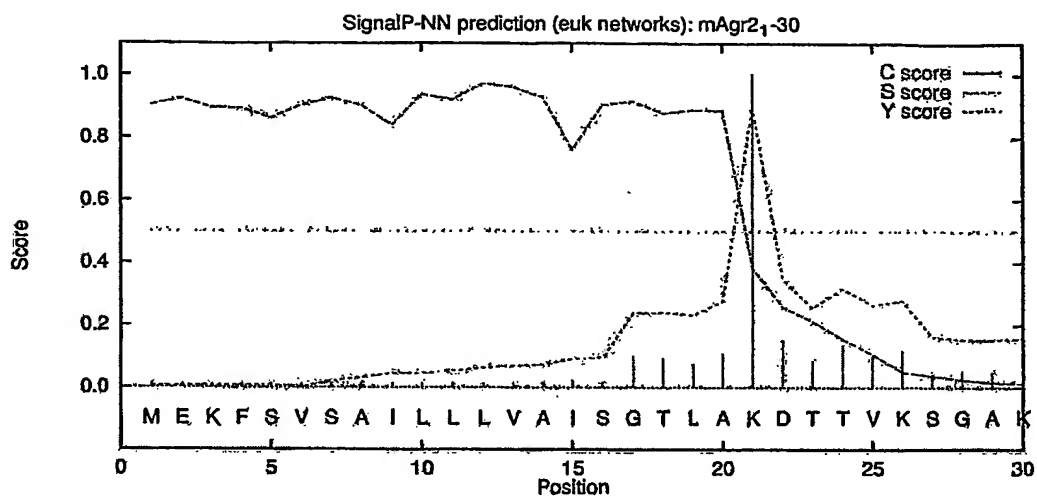
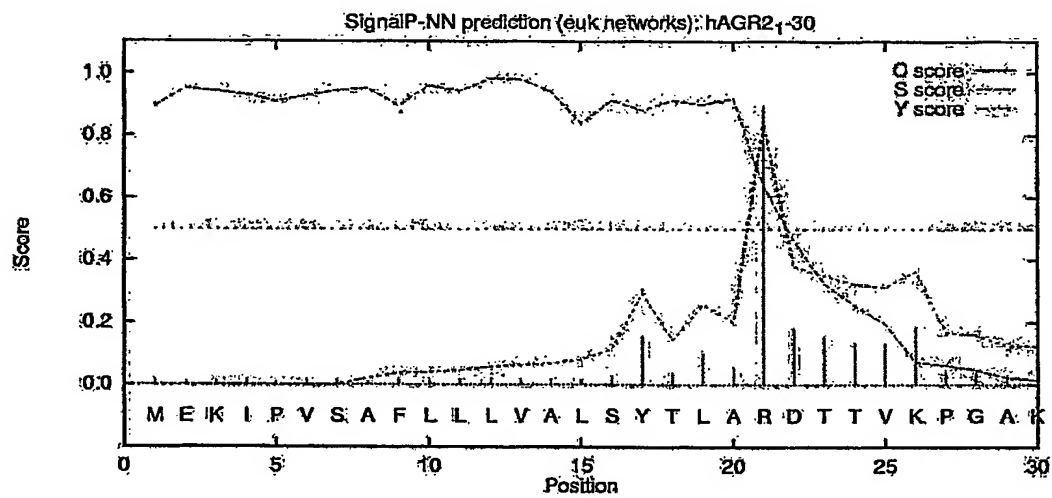
Figure 15A.**Figure 15B.**

Figure 16.

Software used:

- MultAlin via <http://prodes.toulouse.inra.fr/multalin/multalin.html> [Corpet. F. (1988), Multiple sequence alignment with hierarchical clustering, Nucl. Acids Res., 16 (22), 10881-10890]
- BOXSHADE 3.21 via http://www.ch.embnet.org/software/BOX_form.html

Mm: Mus musculus; NP_035913

Hs: Homo sapiens; NP_006399

Rn: Rattus norvegicus; derived by Genewise on AC126809

Mm	1	MEKFSVSAILLLVAISGTLAKDTTVKSGAKKDPKDSRPKLPQTL SRGWGDQLIWTQTYEE
Rn	1	MEKFSVSAILLLVAISGTLAKDTTVKSGAKKDPKDSRPKLPQTL SRGWGDQLIWTQTYEE
Hs	1	MEKFSVSAILLLVAISGTLAKDTTVKSGAKKDPKDSRPKLPQTL SRGWGDQLIWTQTYEE
Consensus	1	MEKFSVSAILLLVAISGTLAKDTTVKSGAKKDPKDSRPKLPQTL SRGWGDQLIWTQTYEE

Mm	61	ALYKSKTSNRPLMVIHHLDECPHSQALKKVFAENKEIQKLAEQFVLLNLVYETTDKHLSP
Rn	61	ALYKSKTSNRPLMVIHHLDECPHSQALKKVFAENKEIQKLAEQFVLLNLVYETTDKHLSP
Hs	61	ALYKSKTSNRPLMVIHHLDECPHSQALKKVFAENKEIQKLAEQFVLLNLVYETTDKHLSP
Consensus	61	ALYKSKTSNRPLMVIHHLDECPHSQALKKVFAENKEIQKLAEQFVLLNLVYETTDKHLSP

▼MTZ (VVE)

Mm	121	DGQYVPRIVFVDPSLTVRADITGRYSNRLYAYEPSDTALLYDNMKKALKLLKTEL
Rn	121	DGQYVPRIVFVDPSLTVRADITGRYSNRLYAYEPSDTALLYDNMKKALKLLKTEL
Hs	121	DGQYVPRIVFVDPSLTVRADITGRYSNRLYAYEPSDTALLYDNMKKALKLLKTEL
Consensus	119	DGQYVPRIVFVDPSLTVRADITGRYSNRLYAYEPSDTALLYDNMKKALKLLKTEL

Percentage of identical and similar amino acids:	95.4%
Percentage of identical amino acids:	90.8%

Figure 17.

Software used:

- MultAlin via <http://prodes.toulouse.inra.fr/multalin/multalin.html> [Corpet. F. (1988), Multiple sequence alignment with hierarchical clustering, Nucl. Acids Res., 16 (22), 10881-10890]
- BOXSHADE 3.21 via http://www.ch.embnet.org/software/BOX_form.html

Mm: Mus musculus; NP_035913
 Hs: Homo sapiens; NP_006399
 Rn: Rattus norvegicus; derived by Genewise on AC126809
 Xl: Xenopus laevis; AAL26844

Mm	1	MEKFSVSAIILLVATSGTLAKDTTVKS	SAKKDP	KDSRPKLPQTL	SRGWGDQLIWTQTYEE
Rn	1	MEKFSVSAIILLVATSGTLAKDTTVRS	SGKKDP	KDSRPKLPQTL	SRGWGDQLIWTQTYEE
Hs	1	MEKIPVSAFLLLVATSYTLAKDTTVKS	SAKKDT	KDSRPKLPQTL	SRGWGDQLIWTQTYEE
Xl	1	MEITVLKSLFELLVATSETLAK	KKPQTL	SRGWGDILEWVQTYEE
Consensus	1	MEK..VSAFLLVA.S.TLAK#TTVK.	SAKKD.	KDSRPKLPQTL	SRGWGD#LIWTQTYEE

Mm	61	ALYKSKTSNRPPLMIHHLDEC	PHSQALKKVFAEH	KEIQKLAEQFVLLNLVYETTDKHLSP
Rn	61	ALYKSKTSNRPPLMIHHLDEC	PHSQALKKVFAENKEIQKLAEQFVLLNLVYETTDKHLSP	
Hs	61	ALYKSKTSNKPLMIHHLDEC	PHSQALKKVFAENKEIQKLAEQFVLLNLVYETTDKHLSP	
Xl	45	GLEKAKSENKPLLLINRHH	CPHSQALKKAFAEHOGIQKLAEFFLLNLVYETTDKHLSP	
Consensus	53	ALYKSKTSNKPLS.IHHL##	CPHSQALKKVFAENKEIQKLAE#F!LLNL!Y#TTDKHLSP	

▼MTZ (VVE)

Mm	121	DGOYVPRIVFVDPSLTVRADITGRYSNRLYAYEP	SDTALLYDNM	KKALKLLKTEL
Rn	121	DGOYVPRIVFVDPSLTVRADITGRYSNRLYAYEP	SDTALLHONM	KKALKLLKTEL
Hs	121	DGOYVPRIVFVDPSLTVRADITGRYSNRLYAYEP	ADTALLLDNM	KKALKLLKTEL
Xl	105	DGOYVPRIVFVDPSLTVRADITGRYSNRLYAYEP	ADIDHLEFNM	KKALVLLKTEL
Consensus	104	DGOYVPRIVFVDPSLTVRADITGRYSNRLYAYEP	ADTALL.#NM	KKALKLLKTEL

Percentage of identical and similar amino acids: 82%
 Percentage of identical amino acids: 67%

Figure 18.

Software used:

- MultAlin via <http://prodes.toulouse.inra.fr/multalin/multalin.html> [Corpet. F. (1988), Multiple sequence alignment with hierarchical clustering, Nucl. Acids Res., 16 (22), 10881-10890]
- BOXSHADE 3.21 via http://www.ch.embnet.org/software/BOX_form.html

Mm: *Mus musculus*; NP_035913
 Hs: *Homo sapiens*; NP_006399
 Rn: *Rattus norvegicus*; derived by Genewise on AC126809
 Xl: *Xenopus laevis*; AAL26844
 Ce: *Caenorhabditis elegans*; NP_496599

```

Mm      1 MEKFSVSATLLLVATISGTLAKDTTVKSGAKKDEKDSRPKLPQTLSRGWGDQLIWTQTYEE
Rn      1 MEKFSVSATLLLVATISGTLAKDTTVKSGSKKDEKDSRPKLPQTLSRGWGDQLIWTQTYEE
Hs      1 MEKIPVSATLLLVATISYTLAEDTTVKFSGAKKDEKDSRPKLPQTLSRGWGDQLIWTQTYEE
Xl      1 METVLKSLFFLLVATSFETLAKD.....KKPQTLSRGWGDQLIWTQTYEE
Ce      1 ....MRSLHLLALVSAAYASFDKIKD.....STQNELARGEGLDIAWVK.WED
Consensus 1 MEK..VSA.LLLVA.S.TLAKDTTVK.S.KKD.KDSRPKLE#TLSRGWGD#LIWTQTYE#

```

```

Mm      61 ALYRSKTSNRPPLMVIHHLDECPHSQALKKVFAEH...KEIQKLAEQFVLLNLVY..ETTD
Rn      61 ALYRSKTSNRPPLMVIHHLDECPHSQALKKVFAEN...KEIQKLAEQFVLLNLVY..ETTD
Hs      61 ALYRSKTSNRPPLMVIHHLDECPHSQALKKVFAEN...KEIQKLAEQFVLLNLVY..ETTD
Xl      45 GLEKPKSENKPIILLINHRNICPHSQALKKFAEH...OGIQKLAEQFVLLNLVY..ETTD
Ce      45 ALETALDITKPIELLINKSWCHACKALKKTEQASNAKKAFFKLSEHFVWNTEDDDPEFE
Consensus 50 ALYRSKTS#KPLM.IHHLDECPHSQALKKVFA#....KEIQKLAEQF!$LNLVY..#TT#

```

▼MTZ (VVE)

```

Mm      116 KHLSPDGQYVPRIVEVDPSLTVRADITGRYSN.RLYAYEPSDTALLYDNMKKALKLLKTE
Rn      116 KHLSPDGQYVPRIVEVDPSLTVRADITGRYSN.RLYAYEPSDTALLDNMKKALKLLKTE
Hs      116 KHLSPDGQYVPRIVEVDPSLTVRADITGRYSN.RLYAYEPSDTALLYDNMKKALKLLKTE
Xl      100 KNLQLDGQYVPRIVEVDPSLTVRADITGRYSN.HQYTFEPADIDHLEENMKKALVLLKTE
Ce      105 EEYRPDGKYLIPRLIFIDKNGDILQEFKNKAEYKNYAYYYSSPADILNSMKDVLKHFGVD
Consensus 97 KHLSPDGQY!PRIVEVDPSLTVRA#ITGRYS#.RLYAYEPSDTALL.#NMKKALKLLKT#

```

```

Mm      175 L.....
Rn      175 L.....
Hs      175 L.....
Xl      159 L.....
Ce      165 LPEAKRGDKLKPKKPEGKKKEL
Consensus 150 L.....

```

Percentage of identical and similar amino acids: 32%
 Percentage of identical amino acids: 46%

Figure 19.

mRNA regulation
[fold change relative to
reference marker ALAS]

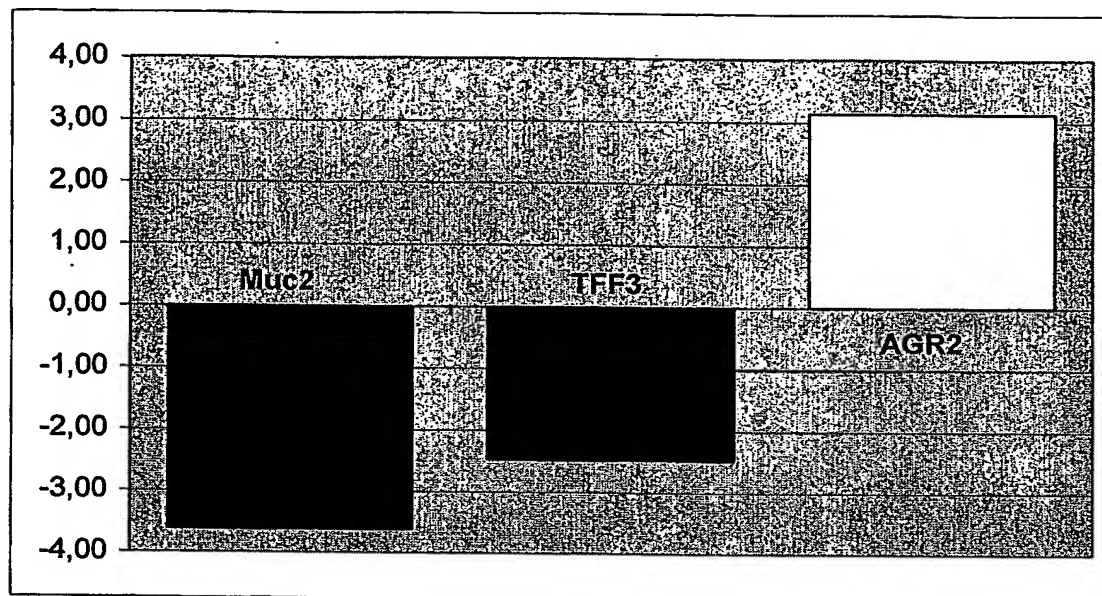
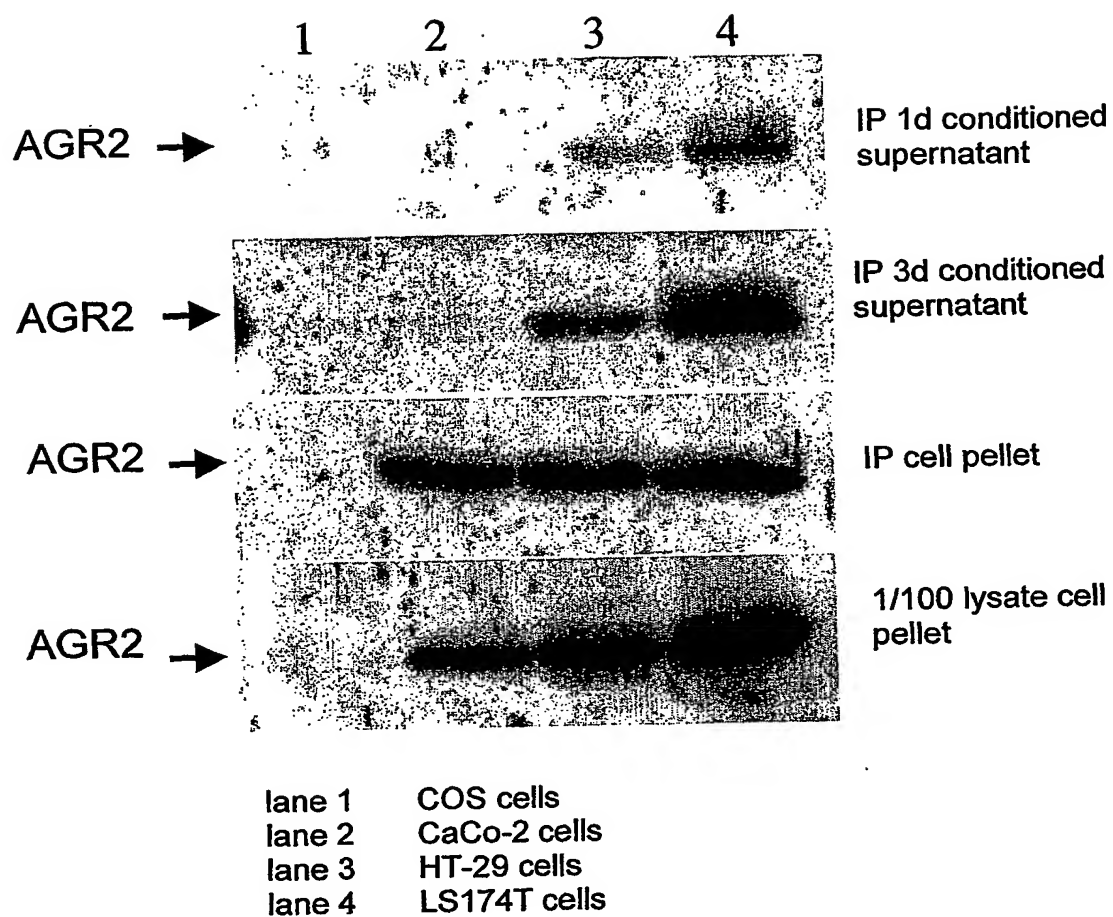


Figure 20.

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